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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/734,801	12/12/2003	Robert W. King	PH7171 DIV	3906

23914 7590 05/10/2006

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 05/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/734,801	KING ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-22,25-28,30,31,33,34 and 38-42* is/are pending in the application.

4a) Of the above claim(s) *14-21 and 40-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22,25-28,30,31,33,34,38 and 39* is/are rejected.

7)☒ Claim(s) *39* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Please vacate the previous office action because it contains a new ground rejection that should make the office action non-Final instead of the Final. The examiner apologizes for the confusing caused by the inadvertent mistake.

Response to Amendment

This is a response to the amendment filed 01/19/2006. Claims 22, 25, have been amended. Claims 23, 24, 29, 32 and 35-37 have been canceled. Claims 14-21 and 40-42 have been withdrawn from the consideration. Claims 14-22, 25-28, 30, 31, 33-34, 38-42 are pending. Claims 22, 25-28, 30-31, 33, 34, 38, 39 are considered before the examiner.

Please note any ground of rejection(s) that has not been repeated is removed. Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 22, 25-28, 30-31, 33, 34, 38, 39 are still rejected under 35 U.S.C. 112, first paragraph under scope of enablement on the same ground as stated in the previous office action.

3. Applicants traverse the rejection and submit that claim 22 has been amended to recite that the cell is transfected with cDAN encoding the RdRp (i.e. HCV) enzyme. Accordingly, the alleged enablement issued should be withdrawn.

4. Applicants' argument has been fully considered; however, it was not found persuasive because the amendment of claim 22 does not cite the cell transfected with a cDAN encoding a RdRp enzyme. To the contrary, it has been amended to an even more broader scope that read on the claimed method is able to be used for identifying a compound or condition which inhibits the replication any genomic sequence of HCV by using a cDNA encoding HCV without limiting that

said HCV cDAN is a full length cDAN of HCV or at least the cDNA of HCV encoding a NS5B polypeptide having a HCV RdRp enzyme. Because the broad scope of new amendments of "a genomic sequence of HCV" and cDNA of HCV" can be reasonably interpreted as a full length of genomic nucleic acid sequence of the HCV genome or just one or couple of nucleic acids of HCV genomic or cDNA sequence. It therefore, still has an enablement issue for the reason set forth bellow:

5. 1). The specification does not provide a sufficient evidence or adequate Guidance for supporting the broad scope of claims read on a method for identifying a compound or condition which inhibits the replication any genomic sequence of HCV by using a cDNA encoding HCV without limiting that said inhibitory effect is dependent on the inhibition of HCV RdRp enzyme;

6. 2). It is still unpredictable for using said antisense reporter system to identify a compound or condition for inhibiting the replication of a genomic sequence of HCV using any cDNA encoding HCV sequence without limiting that said inhibitory effect is dependent on the inhibition of HCV RdRp enzyme, because the working condition of said antisense reporter system relays on the HCV RdRp enzyme to synthesize the complementary (+) strand of said reporter gene that encodes the translatable reporter gene product as evidenced by Hagedron (US patent No. 6,461,845B1 see lines 16-48 on column 22). Therefore, without said RdRp enzyme, the whole system would not be able to be turned on.

7. **New ground rejections:**

Claim Objections

8. Claim 39 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In the instant case claim 39 fails to further limit the claimed subject matter since claim 24 that current claim 39 depends on is canceled.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 22, 25-28, 30-31, 33, 34, 38, 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claim 22 is vague and indefinite in that it is unclear about the orientations of each element of the cited construct. Please clarify the orientations for each claimed elements in the construct in a sequential order s from 5' to 3'.

12. Furthermore, claim 22 is vague and indefinite in that it fails to define the metes and bound of the cited "a genomic sequence of HCV".

13. This affects the dependent claims 25-28, 30-31, 33, 34, 38, 39.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 22, 25, 26, 30, 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Hagedorn et al. (US Patent 5,981,247A).

16. Hagedorn et al. teach a method of using a cell line system to screen a potential inhibitor against HCV RdRp enzyme using a cell line that is engineered to expresses both HCV RNA template and antisense reporter gene construct in the presence or absence of a test inhibitor, He teach that the cell line is transiently transfected with a plasmid engineered to express HCV RNA template and also a construct encoding a reporter molecule system, such as alkaline phosphatase or luciferase, wherein said construct is designed to carry the reporter gene coding sequence in antisense orientation that starts with 5' end, a cap site, of HCV sequence, the reporter coding sequence in antisense orientation, an HCV internal ribozyme entry site (IRES) element, also in (-) stand form, a ribozyme sequence in (+) strand, and a polyadenylation site in (+) strand form,

wherein a suitable ribozyme motif is provided by ribozyme of hepatitis δ virus that is used for removing the polyA tail from the 3' end of the (-) and itself prior to the complementary strand of reporter gene synthesis by RdRp enzyme (See columns 13-14, especially lines 38 of column 13 to line 60 of column 14). Hagedorn et al. teach that the agent used for the transfection is lipofection, which is categorized as a liposome mediated transfection protocol. Hagedorn et al. also teach that the cell line used from the transfection is a Baby Hamster Kidney (BHK) cells (See lines 1-136 on column 12). Therefore, the claimed invention is anticipated by the cited reference.

17. Applicants are reminded that the amendment of claim 22 fails to define whether the claimed HCV cDNA encodes a full length HCV or a fragment of HCV, wherein the full length HCV cDNA will inherently encodes the HC RdRp activity. Because in the specification, applicants refer the coding sequence of the viral genome used in the cultured cells or cell lysate can contain the coding sequence of the RNA-dependent RNA polymerase as part of the entire viral genome, or alternatively, it can contain subgenomic fragments of the viral genome.

18. Hence, applicants are reminded again that Patent Office does not have facilities to perform physical comparisons between the claimed product and similar prior art product in turn of the construct encoding the HCVV mRNA template disclosed by the prior art with the cDNA encoding HCV cited in the current claim 22, the office considered the claimed cDAN encoded the HCV is product either identical or substantially identical to the sequence encoding the HCV RNA cited in the prior art because they both certainly and inherently encode the HC RdRp activity. See In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977) [PTO can require an applicant to establish that a prior art product does not necessarily possess the characteristics of the claimed product when the prior art and claimed products are identical or substantially identical.]

19. While "indirect comparisons, based on established scientific principles, can validly be applied to distinguish a claimed chemical process or product from that disclosed in the prior art," In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 432 (CCPA 1977), the comparisons must be scientifically valid.

20. Patent owner's burden under the circumstances presented herein was described in In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977) as follows:

> Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. . . . Whether the rejection is based on `inherency' under 35 U.S.C. § 102, on `prima facie obviousness' under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products [footnote omitted].

21. The above rejection is also applied by other patents by Hagedorn et al. (6,461,845B1, see columns 21-22) and (6,248,589B1, see columns 13-14) as 102 (e) as evidenced by the disclosures at the same sections for the same reasons as stated above.

Claim Rejections - 35 USC § 103

22. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

23. Claims 22, 25-28, 30-31, 33, 34, 38, 39 are still rejected under 35 U.S.C. 103(a) as being unpatentable over Hagedorn et al. (US patent (US Patent 5,981,247A), Kovelman et al. (US Patent No. 6,326,480B1) and Sherf et al. (US Patent. NO. 5,670,356A) on the same ground as stated in the previous Office Action.

24. Claims invention is drawn to a method of identifying a compound or a condition that inhibits the genomic replication of a virus that depended on RdRp comprising culturing a virus compatible host cell line transfected with the cDNA of such virus and an antisense reporter gene construct comprising an antisense reporter gene sequence flanked at both 5' and 3' ends with 3' and 5' untranslated regions (UTR) of said RdRp virus reverse and antisense orientations

respectively. The said construct further comprises a hepatitis δ virus ribozyme in the antisense orientation operably linked to the 5' UTR sequence, which functions to cleavage the unnecessary part for the activation of the RdRp initiated reporter gene activation. The reporter sequence is preferably selected from the group consisting of luciferase, beta-galctosidase, alkaline phosphatase etc.

25. Hagedorn et al. teach a method of using a cell line system to screen a potential inhibitor against HCV RdRp enzyme using a cell line that is engineered to expresses both HCV RNA template and antisense reporter gene construct in the presence or absence of a test inhibitor, He teach that the cell line is transiently transfected with a plasmid engineered to express HCV RNA template and also a construct encoding a reporter molecule system, such as alkaline phosphatase or luciferase, wherein said construct is designed to carry the reporter gene coding sequence in antisense orientation that starts with 5' end, a cap site, of HCV sequence, the reporter coding sequence in antisense orientation, an HCV internal ribozyme entry site (IRES) element, also in (-) stand form, a ribozyme sequence in (+) strand, and a polyadenylation sitte in (+) strand form, wherein a suitable ribozyme motif is provided by ribozyme of hepatitis δ virus that is used for removing the polyA tail from the 3' end of the (-) and itself prior to the complementary strand of reporter gene synthesis by RdRp enzyme (See columns 13-14, especially lines 38 of column 13 to line 60 of column 14). Hagedorn et al. teach that the agent used for the transfection is lipofection, which is categorized as a liposome mediated transfection protocol. Hagedorn et al. also teach that the cell line used from the transfection is a Baby Hamster Kidney (BHK) cells (See lines 1-136 on column 12). The disclosure of Hagedorn et al. teach the general methodology of each elements required for the claimed method, i.e. use HCV RdRp as key enzyme to control and catalyze a reporter gene expression, wherein both the HCV cDNA and reporter gene expression antisense construct are separately encoded by a constructs and transfected into a cell line. More importantly, Hagedorn et al. also teach the general structure and mechanism of using said cell line system co-transfected with an antisense reporter gene antisense construct and a HCV cDNA sequence encoding HCV RdRp enzyme. This is in contrast to applicants' argument in the response filed on January 19, 2006, that the previous rejection does not considered the invention as whole. The primary reference of Hagedorn et al. cited by this office action meet

almost all general elements of claimed construct in claim 22, expect the minor species of reporter gene, such as luciferase and a particular HCV viral sequence cited in the depended claims.

26. The second reference by Kovelman et al. further teaches how the antisense reporter gene construct is constructed using the HCV 3' and 5' UTR and RdRp gene sequence. Kovelman et al. also specifically teach that the reporter gene is luciferase.

27. Regarding to the utilization of SEQ ID NO: 18, Sherf et al. disclose a reporter gene sequence that is 100 % homology to the reporter gene sequence of SEQ ID NO: 18 in the present Application, the said reporter gene is modified to be more suitable and convenient for diverse applications (See lines 54-55 on col. 2 and Claim 4).

28. Because the method and notion underlined the claimed method is already taught by Hagedorn et al. and Kovelman et al. no matter which reporter gene and which HCV sequence is used as long as the reporter gene sequence is in the antisense orientation and the HCV sequence encoding the RdRp activity, the method for using such system to test an RdRp inhibitor is going to work absence unexpected result to the contrary. Hence, the claimed invention as a whole is still considered as prima facie obvious absence unexpected results.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 7:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bao Qun Li

BAOQUN LI, MD
PATENT EXAMINER

Baoqun Li